Asymmetric Catalysis

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# Propylene Carbonate as a Solvent for Asymmetric Hydrogenations**

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*Dedicated to Professor Rüdiger Selke*

The correct choice of solvent is one of the central problems in synthetic chemistry, for in many cases the physical and toxicological properties of a solvent have a pivotal influence on its use on both the laboratory and industrial scale. Multiphase methods with immiscible solvents allow repeated recycling of the catalyst in homogeneous catalysis.[1] Prominent examples of this ecologically and economically sensible approach include catalyzed reactions in multiphase systems containing water,[2] fluorinated hydrocarbons,[3] supercritical $CO_2$,[4] and ionic liquids (ILs).[5]

Up to now organic cyclic carbonates, in particular propylene carbonate (PC), have not played a role as solvents for asymmetric hydrogenations. The few exceptions in homogeneous catalysis include the platinum-catalyzed hydrosilylation of unsaturated fatty acids investigated by Behr et al.[6] and regioselective, rhodium-catalyzed hydroformylation in PC as solvent.[7] Reetz et al. were successful in stabilizing palladium colloids with PC.[8]

Propylene carbonate is a dipolar aprotic solvent that has previously found application mainly in extractions, electrochemistry, cosmetics, and medicine. In addition to its excellent solvation properties, PC has valuable physical properties such as low viscosity, and it is essentially odorless. Like other organic carbonates PC is usually anhydrous, noncorrosive, nontoxic, and biodegradable.[9] Based on these properties organic carbonates offer a "safe" and environmentally friendly alternative to standard solvents such as $CH_2Cl_2$ and THF, as well as aromatic and toxic solvents.[10] Many alkyl carbonates are available commercially.[11]

In order to investigate the suitability of PC for asymmetric hydrogenations, rhodium-catalyzed asymmetric hydrogenations were initially carried out with a set of common olefins. The commercially available diphosphanes cat*A*Sium M,[12] Me-duphos,[13] binap,[14] tol-binap,[15] and josiphos[16] were used as ligands. The precatalysts were prepared by reaction of the ligands with $[Rh(cod)_2]BF_4$ in PC in situ (cod = 1,5-cyclooctadiene).

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For comparison the hydrogenations were carried out in parallel in MeOH, THF, and $CH_2Cl_2$. The results for methyl α-acetylaminocinnamate and dimethyl itaconate are listed in Table 1 and Table 2. It is clear from these measurements that PC is ideally suited for asymmetric hydrogenation, since similar or even higher enantioselectivities are achieved with comparable reactivity.[17]

***Table 1:*** Rhodium-catalyzed asymmetric hydrogenation of methyl α-acetylaminocinnamate with different phosphane ligands.[a]

| | *ee* [%][b] | | | |
|---|---|---|---|---|
| Ligand | PC | MeOH | THF | $CH_2Cl_2$ |
| cat*A*Sium M | 97 | 94 | 99 | 98 |
| Me-duphos | 99 | 98 | 97 | 98 |
| binap | 43 | 14 | 45 | 32 |
| tol-binap | 50 | 4 | 47 | 35 |
| josiphos | 79 | 77 | 86 | – |

[a] Complexes of the type $[Rh(cod)_2]BF_4$ (L = ligand) were used as catalysts; cat*A*Sium M = 2,3-bis[(2*R*,5*R*)-2,5-dimethylphospholanyl]maleic acid anhydride, Me-duphos = 1,2-bis[(2*R*,5*R*)-2,5-dimethylphospholanyl]benzene, binap = (*R*)-2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl, tol-binap = (*R*)-2,2′-bis(di-*p*-tolylphosphanyl)-1,1′-binaphthyl, josiphos = (*R*)-1-[(*S*)-2-diphenylphosphanyl)ferrocenyl]ethyldicyclohexylphosphane. Substrate/cat. 100:1, 7.5 mL solvent, $p(H_2) = 1$ bar (isobar), 25 °C. [b] Determined by GC, 25 m γ-cyclodextrin, lipodex E (Machery und Nagel), silica, 130 °C, complete conversion after 3 h.

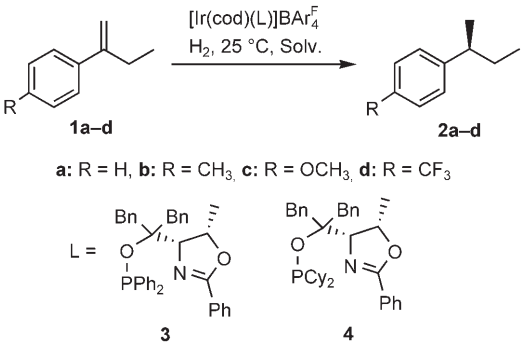
***Table 2:*** Rhodium-catalyzed asymmetric hydrogenation of dimethyl itaconate with different phosphane ligands.[a]

| | *ee* [%][b] | | | |
|---|---|---|---|---|
| Ligand | PC | MeOH | THF | $CH_2Cl_2$ |
| cat*A*Sium M | 95 | 60 | 86 | 98 |
| Me-duphos | 97 | 95 | 97 | 80 |
| binap | 73 | 4 | 19 | 77 |
| tol-binap | 78 | 0 | 5 | 75 |
| josiphos | 99 | 88 | 92 | – |

[a] Complexes of the type $[Rh(cod)_2]BF_4$ (L = ligand) were used as catalysts; substrate/cat. 100:1, 7.5 mL solvent, $p(H_2) = 1$ bar (isobar), 25 °C. [b] Determined by GC, 25 m γ-cyclodextrin, lipodex E (Machery und Nagel), silica, 130 °C, complete conversion after 3 h.

Since PC is not miscible with nonpolar solvents, a two-phase reaction would allow catalyst recycling. The requirement is that the catalyst is soluble in PC and the product is more soluble in the nonpolar solvent than in PC. This is not the case for the amino acid and dicarboxylate in Tables 1 and 2. In contrast, in the hydrogenation of nonfunctionalized

olefins, the alkanes formed are highly soluble in hexane. Iridium complexes with the oxazoline phosphites **3** and **4** as ligands were used as catalysts (Scheme 1);[18] these ligands are known to be suitable for the hydrogenation of styrene




***Scheme 1.*** Asymmetric hydrogenation of *p*-substituted α-ethylstyrene.

derivatives such as **1a–d** based on the work of Pfaltz et al.[19] As can be seen from Table 3, similar enantioselectivity values were obtained in PC, although reaction times were significantly greater in PC than in $CH_2Cl_2$. Most results show the known dependency of enantioselectivity on hydrogen pressure.[19]

***Table 3:*** Iridium-catalyzed asymmetric hydrogenation of styrene derivatives in PC and $CH_2Cl_2$.[a]

| Substr. | Solv. | $H_2$ [atm] | [Ir(cod)(**3**)]BAr$^F_4$ | | [Ir(cod)(**4**)]BAr$^F_4$ | |
|---|---|---|---|---|---|---|
| | | | *t* [h][b] | *ee* [%][c] | *t* [h][b] | *ee* [%][c] |
| **1a** | PC | 50 | 4 | 61 (*S*) | 4 | 76 (*S*) |
| **1a** | $CH_2Cl_2$ | 50 | 3 | 64 (*S*) | 3 | 52 (*S*) |
| **1a** | PC | 1 | 6 | 46 (*S*) | 4 | 83 (*S*) |
| **1a** | $CH_2Cl_2$ | 1 | 0.1 | 78 (*S*) | 0.1 | 86 (*S*) |
| **1b** | PC | 50 | 4 | 62 (*S*) | 4 | 78 (*S*) |
| **1b** | $CH_2Cl_2$ | 50 | 1 | 73 (*S*)[d] | 2 | 56 (*S*)[d] |
| **1b** | PC | 1 | 7 | 47 (*S*) | 2 | 85 (*S*) |
| **1b** | $CH_2Cl_2$ | 1 | 0.5 | 88 (*S*)[d] | 0.5 | 91 (*S*)[d] |
| **1c** | PC | 50 | 4 | 61 (*S*) | 4 | 74 (*S*) |
| **1c** | $CH_2Cl_2$ | 50 | 1 | 71 (*S*)[d] | 2 | 58 (*S*)[d] |
| **1c** | PC | 1 | 6 | 54 (*S*) | 2 | 82 (*S*) |
| **1c** | $CH_2Cl_2$ | 1 | 0.5 | 90 (*S*)[d] | 0.5 | 94 (*S*)[d] |
| **1d** | PC | 50 | 4 | 30 (*S*) | 4 | 74 (*S*) |
| **1d** | $CH_2Cl_2$ | 50 | 1 | 46 (*S*)[d] | 2 | 54 (*S*)[d] |
| **1d** | PC | 1 | 7 | 5 (*S*) | 6 | 66 (*S*) |
| **1d** | $CH_2Cl_2$ | 1 | 0.5 | 59 (*S*)[d] | 0.5 | 88 (*S*)[d] |

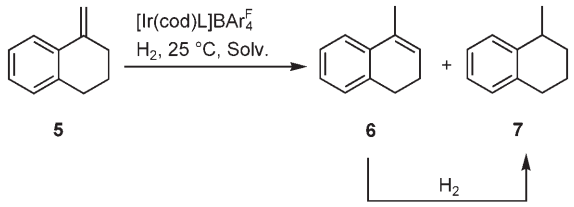
[a] Conditions: 0.4 mmol substrate, 0.004 mmol [Ir(cod)L]BAr$^F_4$, 2 or 8 mL solvent (Solv.), 25 °C. [b] Time for complete conversion. [c] Determined by GC or HPLC. [d] Data from Ref. [19].

In Table 4 the results of a detailed study of the hydrogenation of 1-methylene-1,2,3,4-tetrahydronaphthalene (**5**; Scheme 2) at different hydrogen pressures and temperatures are compared with the results obtained in $CH_2Cl_2$. The chiral product **7** is formed in this reaction as well as the isomerized olefin **6** as an intermediate, which can also be hydrogenated. The hydrogenation of **5** under normal pressure leads to a mixture of **6** and **7** with conversions of 74–100 %. The fraction

***Table 4:*** Iridium-catalyzed asymmetric hydrogenation of **5** in PC and $CH_2Cl_2$.[a]

| Lig. | Solv. | $H_2$ [atm] | *t* [h] | Conv. [%][b] | **6**/**7**[b] | *ee* [%][c] |
|---|---|---|---|---|---|---|
| **3** | PC | 50 | 4 | 100 | 7:93 | 8.3 (*R*) |
| **3** | $CH_2Cl_2$ | 50 | 3 | 100 | 0:100 | 25.7 (*S*) |
| **3** | PC | 1 | 20 | 85 | 62:38 | 3.5 (*R*) |
| **3** | $CH_2Cl_2$ | 1 | 3 | 85 | 50:50 | 28.6 (*S*) |
| **4** | PC | 50 | 4 | 100 | 13:87 | 81.3 (*R*) |
| | | | 8 | 100 | 4:96 | 82.1 (*R*) |
| **4** | PC | 85 | 4 | 100 | 5:95 | 82.1 (*R*) |
| **4** | PC | 100 | 4 | 100 | 3:97 | 82.4 (*R*) |
| **4** | $CH_2Cl_2$ | 50 | 3 | 100 | 0:100 | 16.9 (*R*) |
| **4** | PC | 1 | 20 | 74 | 63:37 | 73.2 (*R*) |
| **4** | $CH_2Cl_2$ | 1 | 3 | 100 | 71:29 | 46.3 (*R*) |

[a] Conditions: 0.4 mmol substrate, 0.004 mmol [Ir(cod)L]BAr$^F_4$, 2 or 8 mL LM, 25 °C. [b] Determined by NMR spectroscopy and GC on chiral phase. [c] Determined by GC on chiral phase.

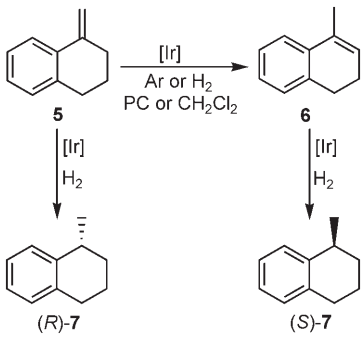



***Scheme 2.*** Asymmetric hydrogenation of 1-methylene-1,2,3,4-tetrahydronaphthalene (**5**).

of the hydrogenation product **7** is usually higher for reactions in $CH_2Cl_2$ than those in PC.

Only very low enantioselectivities were obtained with the use of [Ir(cod)(**3**)]BAr$^F_4$ (BAr$^F_4$ = B(C$_6$H$_3$(CF$_3$)$_2$)$_4$); the best value in $CH_2Cl_2$ was about 28.6 % *ee*. For the hydrogenation with iridium catalysts with the ligand **4** the results in PC were significantly better than those in $CH_2Cl_2$ (increase by about 60 % *ee*). Further improvement to 82.4 % *ee* was obtained with an increase in pressure.

To explain these differences, the isomerization of the external olefin **5** to the internal olefin **6** was investigated initially in the presence of the iridium catalyst but without hydrogen atmosphere (Scheme 3). DFT calculations confirm that **6** is significantly more stable than **5** with its exocyclic double bond.[20] NMR spectroscopic investigations show that the isomerization proceeds more slowly in PC than in $CH_2Cl_2$.[21]




***Scheme 3.*** Studies on the isomerization and hydrogenation of olefins.

By use of the same catalyst, products with opposite configurations are obtained in the hydrogenation of **5** and **6**. The exocyclic olefin is almost exclusively stereoselectively hydrogenated in PC. In contrast, the parallel hydrogenation of **5** and **6** in $CH_2Cl_2$ leads to a mixture of *R* and *S* products and thus to a lower enantioselectivity.[22]

The use of PC would be especially beneficial if the separation of the expensive catalyst in a two-phase mixture were possible. The yellow iridium complex [Ir(cod)(**4**)]$BAr^F_4$ (Figure 1) is located exclusively in the PC phase.

***Figure 1.*** Two-phase system composed of *n*-hexane and PC with [Ir(cod)(**4**)]$BAr^F_4$.

In a typical experiment olefin **5** was hydrogenated in PC and the product was removed by extraction with *n*-hexane. The catalyst can be used up to five times without significant loss in enantioselectivity or an increase in the formation of isomer **6** (Table 5), although an increase in reaction time was observed. The iridium complex probably passes in part into the hexane phase, which could explain the loss in reactivity on repeated use. Modification of the ligand to improve catalyst solubility in PC could be of help.

***Table 5:*** Recycling experiments with the catalyst [Ir(cod)(**4**)]$BAr^F_4$ and olefin **5** as substrate in PC.[a]

| Cycle[b] | *t* [h] | Conv. [%] | **6**/**7**[c] | *ee* [%] |
|---|---|---|---|---|
| 1 | 4 | 100 | 1.5:98.5 | 83.1 (*R*) |
| 2 | 6 | 100 | 3:97 | 84.6 (*R*) |
| 3 | 20 | 100 | 2:98 | 83.7 (*R*) |
| 4 | 20 | 100 | 1.5:98.5 | 83.4 (*R*) |
| 5 | 20 | 100 | 1.5:98.5 | 83.4 (*R*) |
| 6 | 20 | 100 | 2:98 | 79.2 (*R*) |
| 7 | 20 | 85 | 4.5:95.5 | 58.8 (*R*) |
| 8 | 20 | 63 | 5:95 | 50.5 (*R*) |

[a] Conditions: 0.4 mmol substrate, 0.004 mmol [Ir(cod)(**4**)]$BAr^F_4$, $p(H_2) = 85$ bar, 2 mL LM, 25 °C. [b] The catalyst was reused after liquid–liquid extraction with *n*-hexane. [c] Determined by NMR spectroscopy and GC on chiral phase.

The results illustrate the considerable potential of PC in asymmetric hydrogenation. In the reaction of functionalized olefins, the results obtained are similar to or better than those obtained in standard solvents. The asymmetric hydrogenation of nonfunctionalized olefins appears particularly interesting, since then a nonpolar product is formed which can be removed by extraction and the catalyst can be used repeatedly. Further asymmetric catalysis in PC and other organic carbonates is currently under investigation.

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[1] a) *Chemistry in Alternative Reaction Media*, Wiley, Chichester, **2004**; b) *Multiphase Homogeneous Catalysis* (Eds.: B. Cornils, W. A. Herrmann, I. T. Horvath, W. Leitner, S. Mecking, H. Olivier-Bourbigou, D. Vogt), Wiley-VCH, Weinheim, **2005**.
[2] *Aqueous-Phase Organometallic Catalysis* (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, **1998**.
[3] "Fluorous Catalyst": I. Horvath in *Multiphase Homogeneous Catalysis* (Eds.: B. Cornils, W. A. Herrmann, I. T. Horvath, W. Leitner, S. Mecking, H. Olivier-Bourbigou, D. Vogt), Wiley-VCH, Weinheim, **2005**, p. 339–404.
[4] "Catalysis Using Supercritical Solvents": W. Leitner, A. M. Scurto, C. M. Gordon, P. G. Jessop, D. J. Cole-Hamilton, T. Kunene, P. B. Webb, K. Burgemeister, M. Poliakoff in *Multiphase Homogeneous Catalysis* (Eds.: B. Cornils, W. A. Herrmann, I. T. Horvath, W. Leitner, S. Mecking, H. Olivier-Bourbigou, D. Vogt), Wiley-VCH, Weinheim, **2005**, p. 605–750.
[5] *Ionic Liquids in Synthesis* (Eds.: P. Wasserscheid, T. Welton), Wiley-VCH, Weinheim, **2003**.
[6] a) A. Behr, F. Naendrup, D. Obst, *Eur. J. Lipid Sci. Technol.* **2002**, 104, 161–166; b) A. Behr, N. Tosly, *Chem. Eng. Technol.* **2000**, *23*, 122–125; c) A. Behr, F. Naendrup, D. Obst, *Adv. Synth. Catal.* **2002**, *344*, 1142–1145.
[7] a) A. Behr, D. Obst, C. Schulte, T. Schosser, *J. Mol. Catal. A* **2003**, *197*, 115–126; b) A. Behr, D. Obst, B. Turkowski, *J. Mol. Catal. A* **2005**, *226*, 215–219.
[8] M. T. Reetz, G. Lohner, *Chem. Commun.* **1996**, 1921–1922.
[9] Selected properties of PC: m.p. −48 °C; b.p. 242 °C; vapor pressure: 0.045 mm Hg at 25 °C; solubility in water: 175.00 mg $L^{-1}$ at 25 °C; stable in water at pH 4, decomposition begins at higher pH values and at higher temperatures; UV stable; totally biodegradable; $LC_{50} = 480$ mg $L^{-1}$ (fish, butylene carbonate); $EC_{50} = > 5000$ mg $kg^{-1}$ (invertebrates); $EC_{50} = > 929$ mg $kg^{-1}$ (aquatic plants); $EC_{50} = > 5000$ mg $kg^{-1}$ (acute toxicity, oral); $EC_{50} = > 3000$ mg $kg^{-1}$ (acute toxicity, dermal); no gentotoxicity; repeated administration to rats (male/female): $> 5000$ mg $kg^{-1}$ (oral); repeated administration to rats (male/female): $> 100$ mg $m^{-3}$ (inhalation.
[10] BASF recently presented a study in which PC and cresol were compared as solvents in the covering of copper wire from both economic and ecological standpoints. For most of the properties investigated PC was clearly superior. http://www.corporate.basf.com/en/sustainability.
[11] For example, the Huntsman Corporation produces roughly 32000 t alkyl carbonates per annum by ring-opening of the respective epoxide. http://www.huntsman.com.
[12] J. Holz, O. Zayas, H. Jiao, W. Baumann, A. Spannenberg, A. Monsees, T. H. Riermeier, J. Almena, R. Kadyrov, A. Börner, *Chem. Eur. J.* **2006**, *12*, 5001–5013.
[13] M. J. Burk, *J. Am. Chem. Soc.* **1991**, *113*, 8518–8519.
[14] A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi, R. Noyori, *J. Am. Chem. Soc.* **1980**, *102*, 7932–7934.

  

[15] K. Mashima, K. Kusano, N. Sato, Y. Matsumura, K. Nozaki, H. Kumobayshi, N. Sayo, Y. Hori, T. Ishizaki, S. Akutagawa, H. Takaya, *J. Org. Chem.* **1994**, *59*, 3064 – 3075.
[16] A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, A. Tijani, *J. Am. Chem. Soc.* **1994**, *116*, 4062 – 4066.
[17] Comparative measurements on the hydrogenation of cyclooctadiene– and norbornadiene–rhodium complexes provided first indications that the catalytically active complex was formed at about the same rate in PC as in other solvents; "Catalyst Inhibition and Deactivation in Homogeneous Hydrogenation": D. Heller, A. H. M. de Vries, J. G. de Vries in *Handbook of Homogeneous Hydrogenation* (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, **2007**, chap. 44.
[18] a) S. Nanchen, A. Pfaltz, *Chem. Eur. J.* **2006**, *12*, 4550 – 4558; b) C. Hedberg, K. Kallstrom, P. Brandt, L. K. Hansen, P. G. Andersson, *J. Am. Chem. Soc.* **2006**, *128*, 2995 – 3001; c) X. Cui, K. Burgess, *Chem. Rev.* **2005**, *105*, 3272 – 3296; d) S. P. Smidt, F. Menges, A. Pfaltz, *Org. Lett.* **2004**, *6*, 2023 – 2026; e) A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem.* **1998**, *110*, 3047 – 3050; *Angew. Chem. Int. Ed.* **1998**, *37*, 2897 – 2899.
[19] a) F. Menges, A. Pfaltz, *Adv. Synth. Catal.* **2002**, *344*, 40 – 44; b) S. McIntyre, E. Hörmann, F. Menges, S. P. Smidt, A. Pfaltz, *Adv. Synth. Catal.* **2005**, *347*, 2 – 3, 282 – 288.
[20] S. Verevkin, B. Schäffner, V. Andrushko, A. Börner, unpublished results .
[21] To study the isomerization, samples of the substrate were stirred under argon in the presence of the prehydrogenated precatalyst and then analyzed: PC: 39% (10 min), 83% (1 h); $CH_2Cl_2$: 100% (10 min).
[22] Comparable isomerizations have been observed previously in the ruthenium-catalyzed hydrogenation of geraniol: a) Y. Sun, C. LeBlond, J. Wang, D. G. Blackmond, *J. Am. Chem. Soc.* **1995**, *117*, 12647 – 12648; b) Y. Sun, J. Wang, C. LeBlond, R. N. Landau, J. Laquidona, J. R. Sowa Jr, D. G. Blackmond, *J. Mol. Catal. A* **1997**, *115*, 495 – 502.

  